THIS OPINION WAS NOT WRITTEN FOR PUBLICATION

The opinion in support of the decision being entered today (1) was not written for publication in a law journal and (2) is not binding precedent of the Board.

Paper No. 35

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte ALLISON S. CHANG, JAMES E. BOYD,
RICHARD M. JOHNSON and HAROLD O. KOCH

Appeal No. 95-4491
Application 07/864,210[1]

HEARD: March 8, 1999

Before JOHN D. SMITH, HANLON, and LIEBERMAN, Administrative Patent Judges.

HANLON, Administrative Patent Judge.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 from the final

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[1] Application for patent filed April 3, 1992. According to applicants, the application is a continuation of Application 07/451,073, filed December 15, 1989; which is a continuation of Application 06/880,957, filed June 26, 1986, Abandoned; which is a continuation of Application 06/521,575, filed August 9, 1983.

rejection of claims 1, 9, 13, 19, 21, 23-28 and 30-32, all of the claims pending in the application. Claims 1 and 26[2] are illustrative of the subject matter on appeal and read as follows:

1. A method for the protection of human or animal ophthalmic endothelial or epithelial cells subject to trauma during surgery which comprises administering a therapeutically effective amount of a stable, viscous, aqueous composition to said cells during surgery, said aqueous composition consisting essentially of a mixture of chondroitin sulfate and sodium hyaluronate in an aqueous buffer, each of said chondroitin sulfate and said sodium hyaluronate being contained in said aqueous buffer in a concentration of about 0.1 to 50 wt. %, said mixture exhibiting a synergistic viscosity which exceeds the sum of the individual viscosities of said chondroitin sulfate and sodium hyaluronate.

26. A stable, viscous, buffered aqueous solution which comprises a mixture of chondroitin sulfate at a concentration of about 0.1 to 50 wt. % and sodium hyaluronate at a concentration of about 0.1 to 50 wt. %, said mixture exhibiting a synergistic viscosity effect which is sufficient to exceed the sum of the individual viscosities of said chondroitin sulfate and said sodium hyaluronate.

The references relied upon by the examiner are:

Kawano et al. (Kawano)	3,405,120	Oct. 8, 1968
Balazs	4,141,973	Feb. 27, 1979
Pape	4,328,803	May 11, 1982

Japan Pharmaceutical Information Center (Editors), DRUGS IN

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[2]We note that appellants have incorrectly copied claim 26 in the appendix to the appeal brief. A corrected copy of claim 26 has been reproduced in this Decision on Appeal.

JAPAN ETHICAL DRUG EDITION 1975, p. 216 (Tokyo, Japan, Yakugyo Jiho Co., Ltd., Aug. 10, 1975) (referred to hereinafter as "Drugs in Japan").

Chakrabarti et al. (Chakrabarti), "Conformational Studies of Vitreous Polysaccharides," in The Association for Research in Vision and Ophthalmology, Incorporated MEETING SCHEDULE, p. 97 (Sarasota, FL, Spring Meeting, April 25-29, 1974).

The sole issue in this appeal is whether claims 1, 9, 13, 19, 21, 23-28 and 30-32 were properly rejected under 35 U.S.C. § 103 as being unpatentable over the combination of Pape, Balazs, Healon, Kawano, Drugs in Japan, and Chakrabarti.[3]

Discussion

The claims on appeal are directed to a composition comprising a mixture of chondroitin sulfate and sodium hyaluronate in an aqueous buffer (see claim 26) and a method of using the composition for protecting human or animal ophthalmic endothelial or epithelial cells subject to trauma during surgery (see claim 1). The mixture is said to exhibit an unexpectedly synergistic viscosity which exceeds the sum of the individual viscosities of the chondroitin sulfate and sodium hyaluronate.

According to appellants (Specification, pp. 2-3):

[3] Claims 24 and 28 were also finally rejected under 35 U.S.C. § 112, first paragraph, for lack of adequate descriptive support. However, this rejection was withdrawn by the examiner. See Answer, p. 2.

Since human corneal endothelial cells are not known to reproduce, it is of vital importance to

> protect endothelia to prevent cell damage prior to subjection to anticipated trauma, such as surgery
> . . . .
>
> Macromolecules heretofore employed in the protection of corneas include chondroitin sulfate and sodium hyaluronate. The use of a chondroitin sulfate solution for the protection of corneal surface tissue is described in a "CHONDRON" product monogram, Kakan Pharmaceutical Company, Ltd., Tokyo, Japan, 1981. The use of sodium hyaluronate as an aid in ophthalmic surgery is described in a "HEALON" product monogram, Pharmacia Laboratories, Piscataway, New Jersey, 1980.

According to appellants, solutions containing chondroitin sulfate or sodium hyaluronate alone have not met with complete satisfaction (Specification, p. 3). However, appellants' claimed composition, comprising a mixture of chondroitin sulfate and sodium hyaluronate in an aqueous buffer, is said to effectively protect human and animal endothelial and epithelial cells exposed to trauma (Specification, p. 2). More particularly, appellants are said to have discovered that a mixture of chondroitin sulfate and sodium hyaluronate in an aqueous buffer solution exhibits surprisingly high viscosity offering superior protection to corneal surface cells during surgery and aiding in healing after trauma (Specification, p. 3).

According to appellants, viscosity is affected by factors such as molecular weight (Specification, p. 5), buffer solution (Specification, p. 9), temperature (Specification, p. 10), and shear rate (Specification, p. 10). Nevertheless, the mixture of chondroitin sulfate and sodium hyaluronate in an aqueous buffer solution is said to exhibit an unexpectedly synergistic viscosity which exceeds the sum of the individual viscosities of the chondroitin sulfate and sodium hyaluronate.

Rejection under 35 U.S.C. § 103

Claims 1, 9, 13, 19, 21, 23-28 and 30-32 are rejected under 35 U.S.C. § 103 as being unpatentable over the combination of Pape, Balazs, Healon, Kawano, Drugs in Japan and Chakrabarti.

As pointed out above, Healon discloses the use of sodium hyaluronate in ophthalmic surgery.[4] According to Healon, sodium hyaluronate protects corneal endothelium and epithelium both during and after ophthalmic surgery (p. 4). Drugs in

[4] Pape and Balazs, disclosing the use of a sodium salt of hyaluronic acid to protect eye tissue during surgery, are merely cumulative of the teachings in Healon.

Japan[5] discloses the use of sodium chondroitin sulfate to protect the cornea from contact eyeglass injury.[6] The last reference relied upon by the examiner, Chakrabarti, discloses a polysaccharide, ichthyosan, believed to be constituted of hyaluronic acid and chondroitin-like polymer chains.

We agree with appellants that ichthyosan as disclosed in Chakrabarti is a single molecule and not a mixture of sodium hyaluronate and chondroitin sulfate as in the claimed invention (Brief, p. 18; Moll Declaration of April 29, 1993, paragraphs 4-7). Nevertheless, the teachings of Healon and Drugs in Japan alone support a prima facie case of obviousness under 35 U.S.C. § 103.

According to the examiner (Answer, pp. 3-4):

> [I]t is clear from the art of record that both hyaluronic acid and chondroitin sulfate were well known in the art at the time of the instant invention for the protection of eyes. Therefore, a person having ordinary skill in the art at the time

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[5] According to appellants, that portion of Drugs in Japan (p. 216) relied upon by the examiner is a CHONDRON product description. See Application 06/521,575, Paper No. 19; see also Specification, p. 3.

[6] Kawano, disclosing the use of chondroitin sulfate to treat eye diseases, is merely cumulative of the teachings in Drugs in Japan.

> of the instant invention would have been motivate [sic, motivated] to combine hyaluronic acid and chondroitin sulfate and to use the resulting composition for the protection of eyes. The above rejection is based on the well established proposition of patent law that no patentable invention resides in combining old ingredients of known properties where the results obtained thereby are no more than the additive affects [sic, effects] of the ingredients.

We disagree with appellants that the references, namely Healon and Drugs in Japan, disclose different utilities, and therefore, were not properly combined. In contrast to In re Geiger, 815 F.2d 686, 2 USPQ2d 1276 (Fed. Cir. 1987), the teachings in Healon and Drugs in Japan provide a suggestion supporting their combination. Both references disclose that their compositions protect corneal tissue from injury. See In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) (“[i]t is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition which is to be used for the very same purpose"). Furthermore, there is no reason to believe that resulting injury to corneal tissue during surgery differs from injury to corneal tissue caused by other trauma. See

Specification, p. 2 ("This invention relates to compositions for protecting both human and animal endothelial and epithelial cells which are subject to exposure to trauma"). Therefore, one having ordinary skill in the art would have expected a mixture of sodium hyaluronate and chondroitin sulfate to protect corneal tissue from injury caused by surgery or other trauma. See In re O'Farrell, 853 F.2d 894, 904, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988) ("[f]or obviousness under § 103, all that is required is a reasonable expectation of success").

Nevertheless, appellants rely on three declarations (Chang Declarations of July 27, 1984, and August 5, 1985, and Hasskarl Declaration of July 29, 1988) to rebut the prima facie case of obviousness. The Chang Declaration of July 27, 1984, is said to demonstrate that the mixture encompassed by the claims on appeal exhibits an unusually high stability at room temperature (Brief, p. 19).

Viscosity and osmolality for a composition of chondroitin sulfate/sodium hyaluronate were said to have been measured after storage at 4EC and 23EC for up to 183 days. The data at room temperature is said to have been plotted in Figures 1 and

2 attached to the declaration. In comparison, Figure 3 is said to illustrate the osmolality of a chondroitin sulfate solution at room temperature, and Figure 4 is said to illustrate the viscosity of a sodium hyaluronate solution at room temperature.

The declaration and evidence presented in support thereof are inconclusive for several reasons. First, the osmolality of the chondroitin sulfate solution at 4EC and the sodium hyaluronate solution at 4EC and 23EC have not been included. Second, the viscosities of the sodium hyaluronate solution appear to have been plotted on logarithmic graph paper. In contrast, the viscosities of the chondroitin sulfate/sodium

hyaluronate solution appear to have been plotted on linear graph paper. Finally, the viscosities of chondroitin sulfate at 4EC and 23EC have not been included.

However, the Chang Declaration of August 5, 1985, said to demonstrate the surprisingly and unexpectedly high viscosity of the claimed composition, is sufficient to rebut the prima facie case of obviousness. According to Chang (Declaration of August 5, 1985, paragraph 2):

> [A] solution of methyl cellulose was mixed with a solution of chondroitin sulfate. The viscosity of the methyl cellulose solution was 5,857 CPS, and the viscosity of the chondroitin sulfate solution was 3 CPS. When a solution containing both methyl cellulose and chondroitin sulfate was prepared, the viscosity of the mixture was found to be 5,991 CPS. The mixture thus exhibited a viscosity of about 2% greater than the sum of the individual viscosities of methyl cellulose and chondroitin sulfate.

See also Specification, p. 6, line 25-p. 7, line 29. In contrast (Chang Declaration of August 5, 1985, paragraph 3):

> [A] sodium hyaluronate solution was prepared having a viscosity of 58,700 CPS, and a chondroitin sulfate solution having a viscosity of 10 CPS. Surprisingly and unexpectedly solution containing both sodium hyaluronate and chondroitin sulfate was found to have a viscosity of 71,500 CPS. That is, viscosity of the composition of the invention was about 22% greater than the sum of the viscosities of the components.

See also Chang Declaration of August 5, 1985, paragraph 5.

Appellants argue that the examiner's failure to consider the Hasskarl Declaration, said to demonstrate commercial success of the claimed invention, is reversible error (Brief, p. 23). For the reasons set forth above, the Chang Declaration of August 5, 1985, rebuts the prima facie case of obviousness. Therefore, any error by the examiner in failing to consider the Hasskarl Declaration is harmless.

The decision of the examiner is reversed.

REVERSED

JOHN D. SMITH Administrative Patent Judge	)	
ADRIENE LEPIANE HANLON Administrative Patent Judge	)	BOARD OF PATENT APPEALS AND INTERFERENCES
PAUL LIEBERMAN Administrative Patent Judge	)	

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Lowe, Price, LeBlanc & Becker
99 Canal Center Plaza, Suite 300
Alexandria, VA 22314